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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/591,441	01/18/96	QUENTIN MILLET	M XI/P0295US0

EXAMINER

18N2/0514

THOMAS F SQUIRE
LARSON & TAYLOR
727 23RD STREET SOUTH
ARLINGTON VA 22202

ART UNIT	PAPER NUMBER
1813	15

DATE MAILED: 05/14/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☒ NOTICE TO COMPLY SEQUENCE RULES.

Part II SUMMARY OF ACTION

1. ☒ Claims 54-82 are pending in the application.
   Of the above, claims 79-82 are withdrawn from consideration.
2. ☒ Claims 1-53 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 54-78 are rejected.
5. ☐ Claims _____ are objected to.
6. ☒ Claims 54-82 are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☒ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☒ been filed in parent application, serial no. PCT/EP95/04830; filed on 5-30-95.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 2/93)

1. The preliminary amendments filed 18 April 1996, Paper No. 6, and filed 7 February 1997, Paper No. 13, have been entered.

Election/Restriction

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 54-78, drawn to a polypeptide, an isolated DNA fragment, and a pharmaceutical composition of polypeptide.

Group II, claim(s) 79-82, drawn to monoclonal antibody and a pharmaceutical composition of antibody.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons.

Group I is drawn to a polypeptide, an isolated DNA

fragment, and a pharmaceutical composition of polypeptide. Pursuant 37 CFR 1.475(d), these claims are considered by the ISA/US to constitute the main invention, and none of the related group II correspond to the main invention.

The products of Groups I and II do not share the same special technical features because any one of the product of group I and II are structurally and functionally different from each other and each defines a separate invention over the art.

During a telephone conversation with Attorney Thomas Sarro on 29 April 1997 a provisional election was made with traverse to prosecute the invention of I, claims 54-78. Affirmation of this election must be made by applicant in responding to this Office action. Claims 79-82 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37

CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

Priority

3. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of non-provisional application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Specification

4. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the title of the invention, each of the lettered items should be preceded by the headings indicated below.

(a) Title of the Invention.
(b) Cross-References to Related Applications (if any).
© Statement as to rights to inventions made under Federally-sponsored research and development (if any).
(d) Background of the invention.
1. Field of the Invention.
2. Description of the Related Art including information disclosed under 37 CFR 1.97-1.99.
(e) Summary of the Invention.
(f) Brief Description of the Drawing.
(g) Description of the Preferred Embodiment(s).
(h) Claim(s).
(I) Abstract of the Disclosure.

The heading for the Brief Description of the Drawing is missing from page 19, line 10.

Sequence Rules 37 CFR 1.821-1.825

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures.

Page 30, lines 36 and 39 disclose an amino acid sequence of peptides which must comply with the sequence rules.

Applicant is given the period set for response to this Office action from the date of this letter within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for response beyond the SIX MONTH statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

6. The specification is objected to because it does not comply with 37 C.F.R. 1.821 (d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification wherever a reference is made to that sequence. See M.P.E.P. 2422.04.

The legends for figures 1-4 and 8-10 (on page 19, lines 12-35) must identify each of the sequences disclosed in figures 1-4 and 8-10 with the individual SEQ ID NO:. It is not sufficient to identity the sequence as a fragment of larger SEQ ID NO: because

each sequence disclosure has its own SEQ ID NO:. Pages 20, 24, and 30 also disclose sequences which must be identified by its SEQ ID NO:. Any references to sequences in the specification or the claims must be identified with an appropriate SEQ ID NO:.

Claim Rejections - 35 USC § 112

7. Claims 54-78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a Tbp2 receptor of SEQ ID NO:2 and 4, does not reasonably provide the full scope of enablement for derivatives of Tbp2 receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 54-78 encompass Tbp2 derivatives and variants because of the recitation of an "derived". However, the specification fails to teach how to use the derivatives of Tbp2 because the claims are single means claims. A single means claim is a claim which depend on a recited property, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those

known to the inventor (MPEP 2164.08(a)). The specification defines on page 7, lines 36-39, that the term "sequence which is derived from another sequence" to mean a sequence originating form this other sequence by the use of a mental process. Thus, the claims encompass all variants of Tbp2 based on sequence comparisons and mental processes. One skilled in the art cannot predict whether such polypeptides would have any relationship to the TBP2 polypeptide. The state of the art is such that one skilled in the art cannot predict the tertiary structure of protein based on the primary amino acid sequence (Bowie et al.(S)). Thus, it would require undue experimentation to make and use variants with amino acid substitutions in the Tbp2 receptor because one skilled in the art could not predict the effect of the changes due to substitutions on the tertiary structure of the Tbp2 receptor which is necessary to determine if the protein is functional. Furthermore, changes tertiary structure will affect any antibody based on the original epitope of the natural Tbp2 protein found in the bacteria and if the antibody does not recognize the natural Tbp2 protein in the bacteria it cannot be used in diagnostic assay or for vaccination. It would require empirical determination to

determine the all variant combinations which are functional because one skilled in the art cannot predict the which combination of variants of Tbp2 receptor would result in a functional polypeptide. Guidance and working examples directed to the Tbp2 receptor in the specification are not predictive of using *any* variants or derivatives of Tbp2 receptor because the changes in tertiary structure affects the protein function in an unpredictable manner. Therefore, in view of the large extent and unpredictable nature of the experimentation which would be involved, one skilled in the art could not make and use the full scope of the invention as claimed without undue experimentation.

8. Claims 54-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A deposit of the Neisseria meningitidis strain IM2169 or IM2394 is required to enable the invention of claims 54-78. This determination has been made because the claimed strains or vectors have not been fully disclosed or the materials required

to isolate the claimed strains have not been shown to be publicly known and fully available. The specification does not teach how to make the disclosed strains, in a sufficient manner to practice the invention because one skilled in the art could not determine the exact materials necessary to construct the strains. It would require undue experimentation to determine the exact materials necessary to construct the strains. Without a publicly available deposit of the above vectors or strains, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. A suitable deposit for patent purposes is required.

If a deposit has been made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating (a) that the deposit has been made under the terms of the Budapest Treaty; and (b) that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R. § 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then the requirements may be satisfied by an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or by a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and establishing that the following criteria have been met: (a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto; (b) all restrictions imposed by the

depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent; (c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material; (d) a viability statement in accordance with the provisions of 37 C.F.R. § 1.807 is provided; and (e) the deposit will be replaced should it become necessary due to inviability, contamination, or loss of capability to function described in the manner in the specification.

In either case, the identifying information set forth in 37 C.F.R. § 1.809(d) should be added to the specification if it is not already present. See 37 C.F.R. §§ 1.803-1.809 for additional explanation of these requirements.

9. Claims 54-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 54-78 is indefinite for recitation of "stringent conditions" which is a relative term and it is not clear whether the condition is high, moderate, or low stringency condition for hybridization.

Claims 54-78 are indefinite and confusing because SEQ ID NO:1 and 3 are DNA sequences and the claims are to polypeptide thus it is not clear how a maximal homology alignment can be performed between a DNA sequence and an amino acid sequence.

Claims 54-78 are indefinite and confusing because of the

recitation of "maximal homology alignment". The instructions or algorithm for determining sequence identity is missing from the specification. Furthermore, the metes and bounds of the term "homology" have not been clearly set forth neither in the claims nor in the specification. The precise meaning of "homology" in biology is having a common evolutionary origin" (Reeck et al.; R). The paper further explains that homology is a concept of quality or type of relationship between two or more things. Thus, amino acids or nucleotide sequences cannot exhibit a particular quantity or level of homology or percent homology. A more appropriate term is "identity." However, it should be noted that quantitative determination of identity requires subjective determinations for sequences compared. Thus, a specific definition of "identity" must be defined taking into considerations such variables as: complete vs partial sequence and gap distances.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 54-77 rejected under 35 U.S.C. 102(b) as being anticipated by Legrain et al.(AS).

Legrain et al. disclose the Tbp2 protein and DNA sequence form Neisseria meningitidis strains B16B6 and M982 (page 74, Results...; page 76, figure 2; page 78, figure 4). Legrain et al. disclose the tryptic peptide fragments of Tbp2 protein (page 74, paragraph bridging the left and right columns).

The examiner has assumed that SEQ ID NO: 1 and 3 should have been directed to the encoding protein amino acid of SEQ ID NO: 2 and 4. Although not called IM2169 and IM2394, the strains M982 and B16B6 are the same. SEQ ID NO: 2 and 4 are identical to the TBP2 amino acid sequences of Legrain et al.(see attached sequence comparisons). The term "derived" is construed to encompass variants and derivatives.

12. Claims 54-76 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Quentin-Millet et al.(AM).

Quentin-Millet et al. disclose the pharmaceutical vaccine

composition comprising Tbp2 protein from Neisseria meningitidis strains 2169 and 2394 (see abstract).

The examiner has assumed that SEQ ID NO: 1 and 3 should have been directed to the encoding protein amino acid of SEQ ID NO: 2 and 4. Although not called IM2169 and IM2394, the strains 2169 and 2394 are the same. The term "derived" is construed to encompass variants and derivatives. The Tbp2 receptor inherently has the amino acid sequence of SEQ ID NO:2 and 4 because Tbp2 receptor of Quentin-Millet et al. is the same receptor as claimed.

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Quentin-Millet et al.(AN), Stevenson et al.(AR), and Jacobs et al.(AL), is cumulative reference with Quentin-Millet et al.(AM).

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Pak whose telephone number is (703) 305-7038. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be

reached on (703) 308-2957. The fax phone number for this Group is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MDP
Michael D. Pak
1812
29 April 1997

Stephen Walsh
STEPHEN WALSH
SUPERVISORY PATENT EXAMINER
GROUP 1800

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MPSRCH (TM)

****

Release 2.1D John F. Collins, Biocomputing Research Unit.

rch_pp protein - protein database search, using Smith-Waterman algorithm

on: Wed Apr 23 08:05:58 1997; MasPar time 24.91 Seconds
813.564 Million cell updates/sec

Tabular output not generated.

Title: >US-08-591-447-2
Description: (1-711) from US08591447.pep
Perfect Score: 4803
Sequence: 1 MNNPLVNQAAMVLPVFLLSA.....GNSASSATVVFGAKRQQPVQ 711

Scoring table: PAM 150
Gap 11

Searched: 89912 seqs, 28507787 residues

Post-processing: Minimum Match 0%
Listing first 45 summaries

Database: pir50
1:ann1 2:ann2 3:ann3 4:ann4 5:unann1 6:unann2 7:unann3
8:unann4 9:unann5 10:unann6 11:unann7 12:unann8
13:unann9 14:unann10 15:unenc 16:unrev

Statistics: Mean 49.273; Variance 110.985; scale 0.444

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB	ID	Description	Pred. No.
1	4803	100.0	711	7	JN0820	transferrin-binding	0.00e+00
2	1208	25.2	216	16	S61545	transferrin binding	3.11e-191
3	1202	25.0	210	16	S61548	transferrin binding	4.02e-190
4	1062	22.1	213	16	S61549	transferrin binding	3.00e-164
5	1045	21.8	217	16	S61546	transferrin binding	4.07e-161
6	766	15.9	599	7	JN0818	transferrin-binding	3.93e-110
7	612	12.7	625	9	D64107	transferrin binding	1.82e-82
8	491	10.2	216	16	S61544	transferrin binding	3.99e-61
9	469	9.8	593	9	B44796	transferrin-binding	2.69e-57
10	469	9.8	593	9	S27483	transferrin-binding	2.69e-57
11	448	9.3	547	9	S49814	transferrin-binding	1.16e-53
12	420	8.7	547	9	A44796	transferrin-binding	7.62e-49
13	403	8.4	547	9	S49815	transferrin-binding	6.13e-46
14	276	5.7	41	7	S37626	transferrin-binding	7.40e-25
15	129	2.7	660	1	ALBS	alpha-amylase (EC 3.	2.67e-03
16	127	2.6	477	5	S02098	alpha-amylase (EC 3.	4.73e-03
17	125	2.6	477	5	A36709	alpha-amylase (EC 3.	8.32e-03
18	124	2.6	477	1	ALBSN7	alpha-amylase (EC 3.	1.10e-02
19	127	2.6	592	1	ALBSNA	alpha-amylase (EC 3.	4.73e-03
20	113	2.4	35	16	S61547	transferrin binding	2.21e-01
21	110	2.3	127	3	R7SMG	ribosomal protein L1	4.87e-01
22	111	2.3	835	3	A45596	trypomastigote-speci	3.75e-01
23	110	2.3	1054	11	A30239	hydroxymethylglutary	4.87e-01
24	106	2.2	127	7	S49537	ribosomal protein L1	1.36e+00
25	105	2.2	320	5	S59947	chitinase (EC 3.2.1.	1.75e+00
26	106	2.2	370	16	S60187	peridinin-chlorophyl	1.36e+00
27	107	2.2	386	1	CTYMCS	site-specific DNA-me	1.05e+00
28	107	2.2	493	11	S50625	GLO3 protein - yeast	1.05e+00
29	107	2.2	1098	11	S38100	hypothetical protein	1.05e+00
30	107	2.2	1504	11	S51848	hypothetical protein	1.05e+00
31	107	2.2	1758	12	S57015	probable purine nucl	1.05e+00
32	107	2.2	1758	12	S50349	probable purine nucl	1.05e+00
33	102	2.1	134	7	A29065	retinol-binding prot	3.70e+00
34	99	2.1	203	3	JQ1061	glycine-rich protein	7.69e+00
35	102	2.1	281	10	D30191	hypothetical protein	3.70e+00
36	100	2.1	320	3	GERTS	bone sialoprotein pr	6.04e+00
37	100	2.1	369	16	S60186	peridinin-chlorophyl	6.04e+00
38	102	2.1	378	9	S47818	hypothetical protein	3.70e+00
39	101	2.1	453	16	I40750	NTA monooxygenase co	4.73e+00
40	99	2.1	482	10	S31478	alpha-amylase (EC 3.	7.69e+00
41	100	2.1	550	11	S14048	RNA helicase dbp2 -	6.04e+00
42	100	2.1	678	9	S46963	ExeD protein - Aerom	6.04e+00
43	100	2.1	678	9	I39678	exeD protein - Aerom	6.04e+00
44	103	2.1	1217	12	S52714	sericin1B - silkworm	2.89e+00
45	100	2.1	3759	12	A35085	trithorax protein -	6.04e+00

ALIGNMENTS

RESULT 1
ENTRY JN0820 #type complete
TITLE transferrin-binding protein 2 precursor - Neisseria meningitidis (strain M982)
ORGANISM #formal_name Neisseria meningitidis
DATE 03-May-1994 #sequence_revision 03-May-1994 #text_change 23-Aug-1996
ACCESSIONS JN0820; PN0635; S33155
REFERENCE JN0818
#authors Legrain, M.; Mazarin, V.; Irwin, S.W.; Bouchon, B.; Quentin-Millet, M.J.; Jacobs, E.; Schryvers, A.B.
#journal Gene (1993) 130:73-80
#title Cloning and characterization of Neisseria meningitidis genes encoding the transferrin-binding proteins Tbp1 and Tbp2.
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##cross-references EMBL:Z15130
#accession PN0635
##molecule_type protein
##residues 21-33;58-65;144-161;178-190;419-424 ##label LE1
GENETICS
#gene tbp2
CLASSIFICATION #superfamily transferrin receptor
KEYWORDS iron transport; membrane protein; metal binding; receptor
FEATURE
1-20 #domain signal sequence #status predicted #label SIG\
21-711 #product transferrin-binding protein 2 #status predicted #label MAT
SUMMARY #length 711 #molecular-weight 76928 #checksum 7833

SEQ ID NO: 2

Query Match 100.0%; Score 4803; DB 7; Length 711;
Best Local Similarity 100.0%; Pred. No. 0.00e+00;
Matches 711; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy    361 VGSAKTKDKLENGAAASGSTGAAASGGAAGTSSENSKLTTVLDAVELTLNDKKIKNLDNF 420

Db    421 snaaqlvvdgimipllpkdsesgntqadkgknggteftrkfehtpesdkkdaqagtqtng 480
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Db    481 aqtasntagdtngktktyevevccsnlnylkygmltrknsksamqaggnssqadakteqv 540
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Qy    481 AQTASNTAGDTNGKTKTYEVEVCCSNLNYLKYGMLTRKNSKSAMQAGGNSSQADAKTEQV 540

Db    541 eqsmflqgertdekeiptdqnvvyrgswyghiangtswsgnasdkeggnraeftvnfadk 600
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Db    601 kitgkltaenrqaqtftiegmiqgngfegtaktaesgfdldqknttrtpkayitdakvkg 660
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Qy    601 KITGKLTAENRQAQTFTIEGMIQGNGFEGTAKTAESGFDLDQKNTTRTPKAYITDAKVKG 660

Db    661 gfygpkaeelggwfaypgdkqtekatatssdgnsassatvvfgakrqqpvq 711
          ||||||||||||||||||||||||||||||||||||||||||||||||||
Qy    661 GFYGPKAEELGGWFAYPGDKQTEKATATSSDGNSASSATVVFGAKRQQPVQ 711


RESULT    2
ENTRY             S61545     #type complete
TITLE             transferrin binding protein 2 - Neisseria meningitidis
                    (fragment)
ORGANISM          #formal_name Neisseria meningitidis
DATE              27-Apr-1996 #sequence_revision 27-Apr-1996 #text_change
                    27-Apr-1996
ACCESSIONS        S61545
REFERENCE         S61544
  #authors        Rokbi, B.; Maitre-Wilmotte, G.; Mazarin, V.; Fourrichon, L.;
                    Lissolo, L.; Quentin-Millet, M.J.
  #journal        FEMS Microbiol. Lett. (1995) 132:277-283
  #title          Variable sequences in a mosaic-like domain of meningococcal
                    tbp2 encode immunoreactive epitopes.
  #accession      S61545
    ##status           preliminary
    ##residues         1-216 ##label ROK
    ##cross-references EMBL:X88866
SUMMARY           #length 216  #molecular-weight 22548  #checksum 5039

  Query Match           25.2%;  Score 1208;  DB 16;  Length 216;
  Best Local Similarity  86.1%;  Pred. No. 3.11e-191;
  Matches   179;  Conservative   14;  Mismatches  15;  Indels   0;  Gaps   0;

Db      8 gngasggtdaaasngaagtssenskllttvldavelklgdkevqkldnfsnaaqlvvdgim 67
          |:|||:|:|||| |||||||||||||||||||| | || : :|||||||||||||||||||
Qy    373 GAAASGSTGAAASGGAAGTSSENSKLTTVLDAVELTLNDKKIKNLDNFSNAAQLVVDGIM 432

Db     68 ipllpeasesgnnqanqgtnggtaftrkfdhtpesdkkdaqagtqangaqtasntagdtn 127
          |||||  |||||  ||: | |||| |||||:|||||||||||||:|||||||||||||||
Qy    433 IPLLPKDSESGNTQADKGKNGGTEFTRKFEHTPESDKKDAQAGTQTNGAQTASNTAGDTN 492

Db    128 gktktyevevccsnlnylkygmltrknsksamqagesssqadakteqvgqsmflqgertd 187
          ||||||||||||||||||||||||||||||||||||| :|||||||||| ||||||||||
Qy    493 GKTKTYEVEVCCSNLNYLKYGMLTRKNSKSAMQAGGNSSQADAKTEQVEQSMFLQGERTD 552

Db    188 ekeipseqnivyrgswyghiasstswsa 215
          |||||::||:|||||||||||::|||||:
Qy    553 EKEIPTDQNVVYRGSWYGHIANGTSWSG 580


RESULT    3
ENTRY             S61548     #type complete
TITLE             transferrin binding protein 2 - Neisseria meningitidis
                    (fragment)
ORGANISM          #formal_name Neisseria meningitidis
DATE              27-Apr-1996 #sequence_revision 27-Apr-1996 #text_change
                    27-Apr-1996
ACCESSIONS        S61548
REFERENCE         S61544
  #authors        Rokbi, B.; Maitre-Wilmotte, G.; Mazarin, V.; Fourrichon, L.;
                    Lissolo, L.; Quentin-Millet, M.J.
  #journal        FEMS Microbiol. Lett. (1995) 132:277-283
  #title          Variable sequences in a mosaic-like domain of meningococcal
                    tbp2 encode immunoreactive epitopes.
  #accession      S61548
    ##status           preliminary
    ##residues         1-210 ##label ROK
    ##cross-references EMBL:X88869
SUMMARY           #length 210  #molecular-weight 22075  #checksum 6596

  Query Match           25.0%;  Score 1202;  DB 16;  Length 210;
  Best Local Similarity  86.7%;  Pred. No. 4.02e-190;
  Matches   182;  Conservative    9;  Mismatches  19;  Indels   0;  Gaps   0;

Db      1 ngavasggtgaarsngaagqssenskllttvldaveltlndkkiknldnfsnaaqlvvdgi 60
          ||| |||:|||| | |||| ||||||||||||||||||||||||||||||||||||||||
Qy    372 NGAAASGSTGAAASGGAAGTSSENSKLTTVLDAVELTLNDKKIKNLDNFSNAAQLVVDGI 431

Db     61 mipllpeasesgknqanqgtnggtaftrkfnhtpksdekdtqagtaengnpaasntagda 120
          ||||||  ||||: ||: | |||| |||||:||| || ||:|||| ||  :||||||||:
Qy    432 MIPLLPKDSESGNTQADKGKNGGTEFTRKFEHTPESDKKDAQAGTQTNGAQTASNTAGDT 491

Db    121 ngktktyevevccsnlnylkygmltrknsksamqagesssqadakteqvgqsmflqgert 180
          |||||||||||||||||||||||||||||||||||| :|||||||||| ||||||||||
Qy    492 NGKTKTYEVEVCCSNLNYLKYGMLTRKNSKSAMQAGGNSSQADAKTEQVEQSMFLQGERT 551

Db    181 dekeipndqnvvyrgswyghianatswsgn 210
          ||||||| ||||||||||||||||:||||||
Qy    552 DEKEIPTDQNVVYRGSWYGHIANGTSWSGN 581


RESULT    4
ENTRY             S61549     #type complete
TITLE             transferrin binding protein 2 - Neisseria meningitidis
                    (fragment)
ORGANISM          #formal_name Neisseria meningitidis
DATE              27-Apr-1996 #sequence_revision 27-Apr-1996 #text_change
                    27-Apr-1996
ACCESSIONS        S61549
REFERENCE         S61544
  #authors        Rokbi, B.; Maitre-Wilmotte, G.; Mazarin, V.; Fourrichon, L.;
                    Lissolo, L.; Quentin-Millet, M.J.
  #journal        FEMS Microbiol. Lett. (1995) 132:277-283
  #title          Variable sequences in a mosaic-like domain of meningococcal
                    tbp2 encode immunoreactive epitopes.
  #accession      S61549
    ##status           preliminary
    ##residues         1-213 ##label ROK
    ##cross-references EMBL:X88870
SUMMARY           #length 213  #molecular-weight 22751  #checksum 6164

  Query Match           22.1%;  Score 1062;  DB 16;  Length 213;
  Best Local Similarity  81.4%;  Pred. No. 3.00e-164;
  Matches   162;  Conservative   14;  Mismatches  21;  Indels   2;  Gaps   2;
```

****

MPSRCH (TM)

****

Release 2.1D John F. Collins, Biocomputing Research Unit.

MPsrch_pp protein - protein database search, using Smith-Waterman algorithm

Run on: Wed Apr 23 08:11:45 1997; MasPar time 20.67 Seconds
826.086 Million cell updates/sec
Tabular output not generated.

Title: >US-08-591-447-4
Description: (1-599) from US08591447.pep
Perfect Score: 4134
Sequence: 1 MNNPLVNQAAMVLPVFLLSA.....EGKQEKASVVFGAKRQQLVQ 599

Scoring table: PAM 150
Gap 11

Searched: 89912 seqs, 28507787 residues

Post-processing: Minimum Match 0%
Listing first 45 summaries

Database: pir50
1:ann1 2:ann2 3:ann3 4:ann4 5:unann1 6:unann2 7:unann3
8:unann4 9:unann5 10:unann6 11:unann7 12:unann8
13:unann9 14:unann10 15:unenc 16:unrev

Statistics: Mean 48.932; Variance 106.796; scale 0:458

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description	Pred. No.
1	4134	100.0	599	7	JN0818	transferrin-binding	0.00e+00
2	1147	27.7	593	9	B44796	transferrin-binding	5.50e-186
3	1147	27.7	593	9	S27483	transferrin-binding	5.50e-186
4	796	19.3	547	9	S49814	transferrin-binding	1.56e-119
5	782	18.9	547	9	A44796	transferrin-binding	6.54e-117
6	777	18.8	625	9	D64107	transferrin binding	5.64e-116
7	766	18.5	711	7	JN0820	transferrin-binding	6.42e-114
8	757	18.3	547	9	S49815	transferrin-binding	3.08e-112
9	185	4.5	213	16	S61549	transferrin binding	1.99e-11
10	171	4.1	217	16	S61546	transferrin binding	2.31e-09
11	167	4.0	210	16	S61548	transferrin binding	8.77e-09
12	158	3.8	216	16	S61545	transferrin binding	1.69e-07
13	142	3.4	216	16	S61544	transferrin binding	2.74e-05
14	112	2.7	41	7	S37626	transferrin-binding	1.81e-01
15	111	2.7	714	11	S66699	hypothetical protein	2.37e-01
16	108	2.6	827	10	F64512	hypothetical protein	5.31e-01
17	104	2.5	250	11	S61626	hypothetical protein	1.52e+00
18	104	2.5	300	8	JQ0707	methanol oxidation p	1.52e+00
19	105	2.5	351	11	S34261	nodulin-45 - narrow-	1.17e+00
20	104	2.5	452	12	S53906	YMK1 protein - yeast	1.52e+00
21	103	2.5	562	11	S57083	chaperonin TCP1 epsi	1.96e+00
22	104	2.5	863	12	S37040	paramyosin - tapewor	1.52e+00
23	103	2.5	4639	7	A54794	dynein heavy chain,	1.96e+00
24	98	2.4	176	5	S00636	iron-sulfur protein	6.95e+00
25	98	2.4	293	5	JQ0380	proteinase T (EC 3.4	6.95e+00
26	98	2.4	317	9	S10362	flagellar hook-assoc	6.95e+00
27	98	2.4	333	10	D64317	hypothetical protein	6.95e+00
28	99	2.4	407	11	S50870	cell division contro	5.42e+00
29	98	2.4	411	9	E64088	ATP-dependent protea	6.95e+00
30	100	2.4	513	5	A35742	aqualysin (EC 3.4.21	4.22e+00
31	98	2.4	786	8	S28084	env polyprotein - si	6.95e+00
32	101	2.4	956	6	S40304	phosphoenolpyruvate	3.28e+00
33	100	2.4	1318	4	HIBPD7	internal virion prot	4.22e+00
34	94	2.3	180	5	S58619	NADH dehydrogenase (	1.84e+01
35	94	2.3	286	11	JQ2289	floral homeotic gene	1.84e+01
36	95	2.3	400	11	S54642	glycine cleavage T p	1.45e+01
37	95	2.3	403	10	S01828	37K protein precurso	1.45e+01
38	97	2.3	437	11	S05357	hypothetical protein	8.89e+00
39	95	2.3	528	1	TVFVG9	protein-tyrosine kin	1.45e+01
40	95	2.3	541	1	TVCHYS	protein-tyrosine kin	1.45e+01
41	94	2.3	541	5	S31645	protein-tyrosine kin	1.84e+01
42	96	2.3	543	1	TVHUYS	protein-tyrosine kin	1.14e+01
43	96	2.3	845	14	A40016	matrin 3 - rat	1.14e+01
44	97	2.3	959	11	B44402	nuclear pore complex	8.89e+00
45	95	2.3	2201	13	A54774	ATP binding cassette	1.45e+01

ALIGNMENTS

RESULT 1
ENTRY JN0818 #type complete
TITLE transferrin-binding protein 2 precursor - Neisseria meningitidis (strain B16B6)
ORGANISM #formal_name Neisseria meningitidis
DATE 03-May-1994 #sequence_revision 03-May-1994 #text_change 23-Aug-1996
ACCESSIONS JN0818; PN0633; S33153
REFERENCE JN0818
#authors Legrain, M.; Mazarin, V.; Irwin, S.W.; Bouchon, B.; Quentin-Millet, M.J.; Jacobs, E.; Schryvers, A.B.
#journal Gene (1993) 130:73-80
#title Cloning and characterization of Neisseria meningitidis genes encoding the transferrin-binding proteins Tbp1 and Tbp2.
#accession JN0818
##status nucleic acid sequence not shown
##molecule_type DNA
##residues 1-599 ##label LEG
##cross-references EMBL:Z15129
#accession PN0633
##molecule_type protein
##residues 21-34;51-61;158-171;351-361;363-368;378-386;441-456; 564-582 ##label LE1
GENETICS
#gene tbp2
CLASSIFICATION #superfamily transferrin receptor
KEYWORDS iron transport; membrane protein; metal binding
FEATURE
1-20 #domain signal sequence #status predicted #label SIG\
21-599 #product transferrin-binding protein 2 #status predicted #label MAT
SUMMARY #length 599 #molecular-weight 65468 #checksum 382

SEQ ID NO:4

Query Match 100.0%; Score 4134; DB 7; Length 599;
Best Local Similarity 100.0%; Pred. No. 0.00e+00;
Matches 599; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Db      1 mnnplvnqaamvlpvfllsaclggggsfdldsvetvqdmhskpkyedeksqpesqqdvse 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SEQ ID NO:4  1 MNNPLVNQAAMVLPVFLLSACLGGGGSFDLDSVETVQDMHSKPKYEDEKSQPESQQDVSE 60
Db     61 nsgaaygfavklprrnahfnpkykekhkplgsmdwkklqrgepnsfserdelekkrgsse 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy     61 NSGAAYGFAVKLPRRNAHFNPKYKEKHKPLGSMDWKKLQRGEPNSFSERDELEKKRGSSE 120
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```
Db    121 lieskwedgqsrvvgytnftyvrsgyvylnknnidiknnivlfgpdgylyykgkepskel 180
Qy    121 LIESKWEDGQSRVVGYTNFTYVRSGYVYLNKNNIDIKNNIVLFGPDGYLYYKGKEPSKEL 180

Db    181 psekitykgtwdyvtdamekqrfeglgsaaggdksgalsaleegvlrnqaeassghtdfg 240
Qy    181 PSEKITYKGTWDYVTDAMEKQRFEGLGSAAGGDKSGALSALEEGVLRNQAEASSGHTDFG 240

Db    241 mtsefevdfsdktikgtlyrnnritqnnsenkqikttrytiqatlhgnrfkgkalaadkg 300
Qy    241 MTSEFEVDFSDKTIKGTLYRNNRITQNNSENKQIKTTRYTIQATLHGNRFKGKALAADKG 300

Db    301 atngshpfisdsdsleggfygpkgeelagkflsndnkvaavfgakqkdkkdgenaagpat 360
Qy    301 ATNGSHPFISDSDSLEGGFYGPKGEELAGKFLSNDNKVAAVFGAKQKDKKDGENAAGPAT 360

Db    361 etvidayritgeefkkeqidsfgdvkkllvdgvelsllpsegnkaafqheieqngvkatv 420
Qy    361 ETVIDAYRITGEEFKKEQIDSFGDVKKLLVDGVELSLLPSEGNKAAFQHEIEQNGVKATV 420

Db    421 ccsnldymsfgklskenkddmflqgvrtpvsdvaarteanakyrgtwygyiangtswsge 480
Qy    421 CCSNLDYMSFGKLSKENKDDMFLQGVRTPVSDVAARTEANAKYRGTWYGYIANGTSWSGE 480

Db    481 asnqeggnraefdvdfstkkisgtltakdrtspaftitamikdngfsgvaktgengfald 540
Qy    481 ASNQEGGNRAEFDVDFSTKKISGTLTAKDRTSPAFTITAMIKDNGFSGVAKTGENGFALD 540

Db    541 pqntgnshythieatvsggfygknaiemggsfsfpgnapegkqekasvvfgakrqqlvq 599
Qy    541 PQNTGNSHYTHIEATVSGGFYGKNAIEMGGSFSFPGNAPEGKQEKASVVFGAKRQQLVQ 599
```

```
RESULT    2
ENTRY             B44796      #type complete
TITLE             transferrin-binding protein, TfbA - Actinobacillus
                    pleuropneumoniae
ORGANISM          #formal_name Actinobacillus pleuropneumoniae
DATE              24-Mar-1993 #sequence_revision 18-Nov-1994 #text_change
                    18-Nov-1994
ACCESSIONS        B44796
REFERENCE         A44796
  #authors        Gerlach, G.F.; Klashinsky, S.; Anderson, C.; Potter, A.A.;
                    Willson, P.J.
  #journal        Infect. Immun. (1992) 60:3253-3261
  #title          Characterization of two genes encoding distinct
                    transferrin-binding proteins in different Actinobacillus
                    pleuropneumoniae isolates.
  #cross-references MUID:92347999
  #contents       AP37, serotype 17
  #accession      B44796
    ##status           preliminary
    ##molecule_type DNA
    ##residues         1-593 ##label GER
    ##cross-references NCBIN:109737; NCBIP:109738
    ##note             sequence extracted from NCBI backbone
SUMMARY           #length 593  #molecular-weight 65529  #checksum 2440

  Query Match           27.7%;  Score 1147;  DB 9;  Length 593;
  Best Local Similarity  38.3%;  Pred. No. 5.50e-186;
  Matches   237;  Conservative  153;  Mismatches 176;  Indels  53;  Gaps  38;

Db      1 mhfkl-npyalaftslflvacsggkgsfdledvrpnqtakaekattsyqdeetkkktkee 59
Qy      1 MNNPLVNQAAMVLPVFLLSACLGGGGSFDLDSVETVQDMHS-KPK--YEDEKSQPESQQD 57

Db     60 ldklmepalgyetqilrrnkapktetgekrnervvelsedkitklyqesveiiphldeln 119
Qy     58 VSENSGAAYGFAVKLPRRNAHFNPKYKEKHK-PLGSM-DWK--KLQRGEPNSFSERDELE 113

Db    120 gkttsndvyhs--hdsk-rldknrdlkyvrsgyvydgsfneirrndsgfhvfkqgidgyv 176
Qy    114 KKRGSSELIESKWEDGQSRVVGYTNFTYVRSGYVYLNK-NNIDIKNN-IVLF--GPDGYL 169

Db    177 yylgvtpskelpkgkvisykgtwdfvsninlere-idgfdtsgdg-knvsatsitetvnr 234
Qy    170 YYKGKEPSKELPSEK-ITYKGTWDYVTD-AMEKQRFEGLGSAAGGDKSGALSALEEGVLR 227

Db    235 dhkvgeklgdnevkgvahssefavdfdnkkltgslyrngyinrnkaq--ev-tkrysiea 291
Qy    228 NQAEASS-GHTDF-GMT--SEFEVDFSDKTIKGTLYRNNRITQNNSENKQIKTTRYTIQA 283

Db    292 diagnrfrgka-kaek-a--gd-piftdsnyleggfygpkaeemagkfftnnkslfavfa 346
Qy    284 TLHGNRFKGKALAADKGATNGSHPFISDSDSLEGGFYGPKGEELAGKFLSNDNKVAAVFG 343

Db    347 ak-se--nge--t--tteriidatkidltqfnakelnnfgdasvliidgqkidl-agvnf 398
Qy    344 AKQKDKKDGENAAGPATETVIDAYRITGEEFKKEQIDSFGDVKKLLVDGVELSLLPSEGN 403

Db    399 knsktveingktmvavaccsnleymkfgqlwqkegkqqvkdnslflqgertatdkmpa-- 456
Qy    404 KAAFQHEIEQNGVKATVCCSNLDYMSFGKL-SKE-N---KDD-MFLQGVRTPVSDVAART 457

Db    457 ggnykyvgtwdalvskgtnwiaeadnnresgyrtefdvnfsdkkvngklfdkggvnpvft 516
Qy    458 EANAKYRGTWYGYIANGTSWSGEA-SNQEGGNRAEFDVDFSTKKISGTLTAKDRTSPAFT 516

Db    517 vdatingngfigsaktsdsgfaldagssqhgnavfsdikvnggfygptagelggqfh-h- 574
Qy    517 ITAMIKDNGFSGVAKTGENGFALDPQNTGNSHYTHIEATVSGGFYGKNAIEMGGSFSFPG 576

Db    575 ksdngs---vgavfgakrq 590
Qy    577 NAPEGKQEKASVVFGAKRQ 595
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```
RESULT    3
ENTRY             S27483      #type complete
TITLE             transferrin-binding protein - Actinobacillus pleuropneumoniae
ORGANISM          #formal_name Actinobacillus pleuropneumoniae
DATE              06-Jan-1995 #sequence_revision 06-Jan-1995 #text_change
                    06-Jan-1995
ACCESSIONS        S27483
REFERENCE         S27483
  #authors        Gerlach, G.F.; Klashinsky, S.; Anderson, C.; Potter, A.A.;
                    Wilson, P.
  #submission     submitted to the EMBL Data Library, March 1992
  #description    Characterization of an Actinobacillus pleuropneumoniae
                    transferrin-binding protein and its distribution among type
                    strains.
  #accession      S27483
    ##status           preliminary
    ##molecule_type DNA
    ##residues         1-593 ##label GER
    ##cross-references EMBL:M85274
SUMMARY           #length 593  #molecular-weight 65582  #checksum 2644

  Query Match           27.7%;  Score 1147;  DB 9;  Length 593;
  Best Local Similarity  38.4%;  Pred. No. 5.50e-186;
  Matches   238;  Conservative  152;  Mismatches 176;  Indels  53;  Gaps  39;

Db      1 mhfkl-npyalaftslflvacsggkgsfdledvrpnqtakaekattsyqdeetkkktkee 59
Qy      1 MNNPLVNQAAMVLPVFLLSACLGGGGSFDLDSVETVQDMHS-KPK--YEDEKSQPESQQD 57

Db     60 ldklmepalgyetqilrrnkapktetgekrnervvelsedkitklyqesveiiphldeln 119
Qy     58 VSENSGAAYGFAVKLPRRNAHFNPKYKEKHK-PLGSM-DWK--KLQRGEPNSFSERDELE 113

Db    120 gkttsndvyhs--hdsk-rldknrdlkyvrsgyvydgsfneirrndsgfhvfkqgidgyv 176
Qy    114 KKRGSSELIESKWEDGQSRVVGYTNFTYVRSGYVYLNK-NNIDIKNN-IVLF--GPDGYL 169

Db    177 yylgvtpskelpkgkvisykgtwdfvsninlere-idgfdtsgdg-knvsatsitetvnr 234
```

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attach paper NO: 15

Application No.: 591,447

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: A copy of the "Sequence Listing" in computer readable form has been submitted. However, the specification contains sequences not submitted as a copy of the "Sequence Listing" in computer readable form or as a paper copy.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

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